

EXHIBIT B: CLEAN VERSION OF PENDING CLAIMS

U.S. APPLICATION SERIAL NO. 09/616,849

(ATTORNEY DOCKET NO. 9301-044)

(as amended December 26, 2002)

27. (Three Times Amended) A method for evaluating a binding property of a polynucleotide probe comprising a predetermined nucleotide sequence to a target nucleotide sequence, said method comprising determining a ratio of the amount of hybridization of polynucleotides in a first sample to the polynucleotide probe and the amount of hybridization of polynucleotides in a second sample to the polynucleotide probe, wherein:

- (a) the first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence; and
- (b) the second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a sequence that is different from the nucleotide sequences of any other polynucleotide molecules in said plurality of different polynucleotide molecules,

wherein at least 75% of the polynucleotide molecules in said first sample are polynucleotide molecules comprising said target nucleotide sequence, and wherein said ratio is used as a measure of said binding property, thereby evaluating said binding property of said polynucleotide probe.

28. (Amended) The method of claim 27 wherein the predetermined nucleotide sequence of the polynucleotide probe is complementary to at least a hybridizable portion of the target nucleotide sequence in the first sample.

29. (Amended) The method of claim 27 wherein the target polynucleotide sequence in the first sample is a nucleotide sequence of a gene or gene transcript of a cell or organism, or of an mRNA, cDNA or cRNA derived therefrom.

30. (Amended) The method of claim 27 wherein the plurality of different polynucleotide molecules in the second sample comprise nucleotide sequences of a plurality of genes or gene transcripts of a cell or organism.

33. (Twice Amended) The method of claim 27 wherein at least 90% of the polynucleotide molecules in said first sample are said polynucleotide molecules comprising said target nucleotide sequence.

34. (Twice Amended) The method of claim 33 wherein at least 95% of the polynucleotide molecules in said first sample are said polynucleotide molecules comprising said target nucleotide sequence.

35. (Twice Amended) The method of claim 34 wherein at least 99% of the polynucleotide molecules in said first sample are said polynucleotide molecules comprising said target nucleotide sequence.

36. (Twice Amended) The method of claim 27 wherein each different polynucleotide molecule in the second sample does not comprise the target nucleotide sequence.

37. (Amended) The method of claim 36 wherein:

- (a) the target polynucleotide sequence in the first sample is a sequence of a gene or gene transcript of a cell or organism; and
- (b) the second sample comprises a polynucleotide sample from a deletion mutant of the cell or organism,

wherein the deletion mutant of the cell or organism does not express the gene or gene transcript.

38. (Amended) The method of claim 27 wherein the plurality of different polynucleotide molecules in the second sample comprises:

- (a) polynucleotide molecules comprising the target nucleotide sequence, and
- (b) a plurality of different polynucleotide molecules, each comprising a different nucleotide sequence and each not comprising the target nucleotide sequence.

39. (Twice Amended) The method of claim 38 wherein:

- (a) the target nucleotide sequence comprises a sequence of a gene or gene

transcript of a cell or organism; and

- (b) the second sample comprises a polynucleotide sample from a wild-type strain of the cell or organism,

wherein the wild-type strain of the cell or organism expresses the gene or gene transcript.

40. (Amended) The method of claim 27 wherein:

- (a) the first sample further comprises polynucleotide molecules that do not comprise the target nucleotide sequence; and
- (b) the second sample lacks said polynucleotide molecules comprising said target nucleotide sequence.

42. (Twice Amended) The method of claim 40 wherein:

- (a) the target nucleotide sequence is a sequence of a gene or gene transcript of a cell or organism;
- (b) the first sample comprises a polynucleotide sample from a wild-type strain of the cell or organism which expresses the gene or gene transcript; and
- (c) the second sample comprises a polynucleotide sample from a deletion mutant of the cell or organism which does not express the gene or gene transcript.

43. (Amended) The method of claim 27 wherein

- (a) the first sample further comprises polynucleotide molecules that do not comprise the target nucleotide sequence; and
- (b) the second sample comprises:
 - (i) polynucleotide molecules comprising the target nucleotide sequence, and
 - (ii) a plurality of different polynucleotide molecules, each different polynucleotide molecule comprising a different nucleotide sequence and not comprising the target nucleotide sequence,

wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs by at least a factor of two from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence.

44. (Amended) The method of claim 43 wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence by at least a factor of four.

45. (Amended) The method of claim 43 wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence by at least a factor of eight.

46. (Amended) The method of claim 43 wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence by at least a factor of twenty.

47. (Amended) The method of claim 43 wherein the amount of polynucleotide molecules in the first sample comprising the target nucleotide sequence differs from the amount of polynucleotide molecules in the second sample comprising the target nucleotide sequence by at least a factor of 100.

48. (Twice Amended) The method of claim 43 wherein each said polynucleotide molecule that does not comprise the target nucleotide sequence in the first sample is present in the second sample in an amount that differs from the amount of said polynucleotide molecule in the first sample by no more than a factor of 100.

49. (Twice Amended) The method of claim 43 wherein each said polynucleotide molecule that does not comprise the target nucleotide sequence in the first sample is present in the second sample in an amount that differs from the amount of said polynucleotide molecule in the first sample by no more than a factor of 10.

50. (Twice Amended) The method of claim 43 wherein each said polynucleotide

molecule that does not comprise the target nucleotide sequence in the first sample is present in the second sample in an amount that differs from the amount of said polynucleotide molecule in the first sample by no more than 50%.

51. (Twice Amended) The method of claim 43 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than a factor of two.

52. (Twice Amended) The method of claim 43 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 50%.

53. (Twice Amended) The method of claim 43 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 10%.

54. (Twice Amended) The method of claim 43 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 1%.

57. (Three Times Amended) The method of claim 38, 40 or 43 wherein said binding property is a specificity of the polynucleotide probe, wherein said specificity is the amount of said polynucleotide molecules comprising said target nucleotide sequence that bind to said

polynucleotide probe relative to the amount of polynucleotide molecules not comprising said target nucleotide sequence that bind to the probe under the same binding conditions.

58. (Amended) The method of claim 57 wherein the specificity of the polynucleotide probe is determined from a ratio of the amount of hybridization of polynucleotide molecules in the first sample to the polynucleotide probe to the amount of hybridization of polynucleotide molecules in the second sample to the polynucleotide probe.

59. (Amended) The method of claim 27 wherein the polynucleotide molecules in the first sample are detectably labeled.

60. The method of claim 27 wherein the polynucleotide molecules in the second sample are detectably labeled.

61. The method of claim 59 or 60 wherein the polynucleotide molecules are labeled with a fluorescent molecule.

62. (Amended) The method of claim 27 wherein:

- (a) the polynucleotide molecules in the first sample are labeled with a first label;
and
- (b) the polynucleotide molecules in the second sample are labeled with a second label,

the first label being distinguishable from the second label.

63. The method of claim 62 wherein:

the first label is a first fluorescent molecule, and
the second label is a second fluorescent molecule.

64. The method of claim 27 wherein the polynucleotide probe is attached to a surface of a support.

65. The method of claim 27 wherein the polynucleotide probe is one of a plurality of polynucleotide probes.

66. (Amended) The method of claim 65 wherein the plurality of polynucleotide probes comprises polynucleotide probes in an array of polynucleotide probes,

said array having a support with at least one surface and different polynucleotide probes attached to said surface,

wherein each of said different polynucleotide probes attached to said surface is attached to the surface of the support in a different location.

67. (Three Times Amended) A method for evaluating a binding property of a plurality of polynucleotide probes to a target nucleotide sequence wherein each polynucleotide probe in the plurality of polynucleotide probes comprises a predetermined nucleotide sequence,

said method comprising determining a ratio of the amount of hybridization of polynucleotides in a first sample to each polynucleotide probe in the plurality of polynucleotide probes and the amount of hybridization of polynucleotides in a second sample to each polynucleotide probe in the plurality of polynucleotide probes, wherein:

- (a) the first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence; and
- (b) the second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a nucleotide sequence that is different from nucleotide sequence of any other polynucleotide molecules in said plurality of different polynucleotide molecules,

wherein at least 75% of the polynucleotide molecules in said first sample are polynucleotide molecules comprising said target nucleotide sequence, and wherein said ratio is used as a measure of said binding property, thereby evaluating said binding property of each said polynucleotide probe.

68. (Amended) The method of claim 67 wherein the predetermined nucleotide sequence of each polynucleotide probe is complementary to at least a hybridizable portion of

the target nucleotide sequence.

73. The method of claim 67 wherein each polynucleotide probe in the plurality of polynucleotide probes is attached to a surface of a support.

74. (Amended) The method of claim 67 wherein the plurality of polynucleotide probes comprises polynucleotide probes in an array of probes,

said array having a support with at least one surface and different polynucleotide probes attached to said surface,

wherein each of said different polynucleotide probes attached to said surface in the plurality of probes is attached to the surface of the support in a different location.

75. (Twice Amended) The method of claim 67 wherein the first sample comprises two or more different polynucleotide molecules

wherein none of the two or more different polynucleotide molecules hybridizes or cross-hybridizes to a probe that also hybridizes or cross-hybridizes to another one of the two or more different polynucleotide molecules.

84. The method of claim 27 wherein:

polynucleotides in the first sample are labeled with a first label and polynucleotides in the second sample are labeled with a second label that is distinguishable from the first label; and further comprising, prior to said step of comparing the steps of:

- (i) concurrently contacting the polynucleotide probe with the first sample and the second sample under conditions conducive to hybridization, and
- (ii) detecting any binding that occurs between the polynucleotide probe and polynucleotides in the first sample and the second sample.

85. (Amended) The method of claim 84 wherein the second sample lacks polynucleotide molecules of said first sample.

90. (Amended) The method of any one of claims 27-30, 33-40, 42-54, 61-68, 73-75

and 84-85, wherein said polynucleotide molecules comprising said target nucleotide sequence are the same polynucleotide molecule.

91. (New) A method for evaluating a binding property of a plurality of polynucleotide probes to a target nucleotide sequence, said method comprising determining a ratio of the amount of hybridization of polynucleotides in a first sample to each polynucleotide probe in the plurality of polynucleotide probes and the amount of hybridization of polynucleotides in a second sample to each polynucleotide probe in the plurality of polynucleotide probes, wherein:

- (a) said first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence and a plurality of polynucleotide molecules that do not comprise the target nucleotide sequence; and
- (b) said second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a sequence that is different from the nucleotide sequence of any other polynucleotide molecule in said plurality of different polynucleotide molecules, and wherein each different polynucleotide molecule in the second sample does not comprise the target nucleotide sequence

wherein each polynucleotide probe in the plurality of polynucleotide probes comprises a predetermined nucleotide sequence and wherein said ratio is used as a measure of said binding property, thereby evaluating said binding property of said plurality of polynucleotide probes.

92. (New) The method of claim 91 wherein:

- (a) said target nucleotide sequence is a sequence of a gene or gene transcript of a cell or organism;
- (b) said first sample comprises a polynucleotide sample from a wild-type strain of the cell or organism which expresses the gene or gene transcript; and
- (c) said second sample comprises a polynucleotide sample from a deletion mutant of the cell or organism that does not express the gene or gene transcript.

93. (New) A method for evaluating a binding property of a plurality of polynucleotide probes to a target nucleotide sequence, said method comprising determining a ratio of the amount of hybridization of polynucleotides in a first sample to each polynucleotide probe in the plurality of polynucleotide probes and the amount of hybridization of polynucleotides in a second sample to each polynucleotide probe in the plurality of polynucleotide probes, wherein:

- (a) said first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence and a plurality of polynucleotide molecules that do not comprise the target nucleotide sequence; and
- (b) said second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a sequence that is different from the nucleotide sequence of any other polynucleotide molecule in said plurality of different polynucleotide molecules,

wherein each polynucleotide probe in the plurality of polynucleotide probes comprises a predetermined nucleotide sequence and wherein said ratio is used as a measure of said binding property, thereby comparing said binding property of said plurality of polynucleotide probes.

94. (New) The method of claim 93 wherein:

- (a) said target nucleotide sequence comprises a sequence of a gene or gene transcript of a cell or organism; and
- (b) said second sample comprises a polynucleotide sample from a wild-type strain of said cell or organism, wherein the wild-type strain of the cell or organism expresses the gene or gene transcript.

95. (New) The method of claim 93, wherein said second sample comprises:

- (b1) polynucleotide molecules comprising the target nucleotide sequence, and
- (b2) a plurality of different polynucleotide molecules, each different polynucleotide molecule comprising a different nucleotide sequence and not comprising the target nucleotide sequence,

and wherein the amount of polynucleotide molecules in said first sample comprising the target nucleotide sequence differs by at least a factor of two from the amount of polynucleotide molecules in said second sample comprising the target nucleotide sequence.

96. (New) The method of claim 95 wherein the amount of polynucleotide molecules in said first sample comprising said target nucleotide sequence differs from the amount of polynucleotide molecules in said second sample comprising said target nucleotide sequence by at least a factor of four.

97. (New) The method of claim 95 wherein the amount of polynucleotide molecules in said first sample comprising said target nucleotide sequence differs from the amount of polynucleotide molecules in said second sample comprising said target nucleotide sequence by at least a factor of eight.

98. (New) The method of claim 95 wherein the amount of polynucleotide molecules in said first sample comprising said target nucleotide sequence differs from the amount of polynucleotide molecules in said second sample comprising said target nucleotide sequence by at least a factor of twenty.

99. (New) The method of claim 95 wherein the amount of polynucleotide molecules in said first sample comprising said target nucleotide sequence differs from the amount of polynucleotide molecules in said second sample comprising said target nucleotide sequence by at least a factor of 100.

100. (New) The method of claim 95 wherein each said polynucleotide molecule that does not comprise said target nucleotide sequence in said first sample is present in said second sample in an amount that differs from the amount of said polynucleotide molecule in the first sample by no more than 50%.

101. (New) The method of claim 95 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first

sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than a factor of two.

102. (New) The method of claim 95 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 50%.

103. (New) The method of claim 95 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 10%.

104. (New) The method of claim 95 wherein the mean abundance of the polynucleotide molecules that do not comprise the target nucleotide sequence in the first sample differs from the mean abundance of the different polynucleotide molecules that do not comprise the target nucleotide sequence in the plurality of different polynucleotide molecules of the second sample by no more than 1%.